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Evidence Based Approach to Perthes

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Authors' contributions

This work was carried out in collaboration between all authors. Author AS designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors VK and SA managed the literature searches and revised the manuscript. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Perthes is a self-limiting disorder of paediatric hip. The outcome of this disorder is variable. Every aspect of it including, etiology, pathogenesis, pathology, classification, natural course, management and outcome is controversial. There is still no clear guideline for the management of Perthes disease. The aim of treatment is to prevent the head deformity and subsequent secondary osteoarthritis of hip. To maximize the results of containment procedures, measures to unstiffen the hip should be taken. Evidences are there that only a section of involved hips need intervention. Most untreated hips do not require intervention until the age of forty.

Keywords: Perthes disease; management of Perthes disease; paediatric hip.

1. INTRODUCTION

About 100 years ago, literature described a peculiar self limiting affection of hip in which the femoral head underwent bony collapse of proximal femoral epiphysis after avascular necrosis. In recognition of the contributions of Legg in USA, by Jacques Calve in France and by George Perthes in Austria, this condition became known as Legg-Calve-Perthes Disease (LCPD) [1]. There is controversy about almost all its aspects, including etiology, pathogenesis

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management, classification, natural history and even the outcome. These factors have led to heterogeneity of different treatment modalities that ranges from the highly invasive to no treatment [2].

2. EPIDEMIOLOGY

The disease is five times more common in boys of 3-8 years old [1-3]. The age for diagnosis of this disease is usually 4-12 years, with average of 6 years [4]. The '80% rule' is useful; it is said that nearly 80% of the cases are seen in boys, 80% cases have a unilateral presentation and 80% develop it between 4-8 years of age [5]. Its incidence varies from 1:10000 children in USA to 2.97 per 10000 children in south India [6]. Approximately 25% of cases show bilateral involvement [5].

2.1 Etiology

Perthes disease is one of the most common causes of a permanent deformity of the femoral head among paediatric hip disorders [7]. The exact etiology of Perthes disease is still unknown; but considered multifactorial. Many authors consider the changes in femoral head are because of repeated aseptic ischaemia of proximal capital femoral epiphysis [5]. Abnormalities in the ossification centers, together with evidence of fragmentation of the epiphyseal growth plate and metaphyseal expansion are thought to be the pathogenetic causation in the development of hip pain in children with skeletal dysplasias [8].

2.1.1 Genetic factor

The role of genetic factor is still controversial. Literatures reveal the genetic association with expression of HLA-A antigens in lymphocytes of Perthes patients [9]. Genetic factors have been implicated in the etiology of Perthes. Clear differentiation of skeletal dysplasias from Perthes disease requires careful phenotypic and genotypic interpretations. The distinction is important because the prognosis of skeletal dysplasias compared with the several causations of Perthes requires prompt indication for therapeutic intervention is more guarded. *COL2A1* mutations give rise to a spectrum of phenotypes predominantly affecting cartilage and bone from the severe disorders that are Perinatally lethal to the milder conditions that are recognized in the post-natal period and childhood. The milder chondrodysplasias are characterized by disproportionate short stature, eye abnormalities, cleft palate, hearing loss and subsequent development of Perthes like disease [10-13].

2.1.2 Trauma

Though it is being considered that repeated trauma to lateral epiphyseal artery is associated with Perthes disease but the role of trauma is difficult to substantiate as mild trauma is a common part of childhood [1,9].

2.1.3 Growth factor

Several studies have observed that children with Perthes disease are of shorter stature with their age lags 2-3 years behind their chronological age [6, 9,14-15].

2.1.4 Environmental

The variable geographical distribution suggest that environmental factors may be involved with Perthes disease [7,16]. The disease is more common in urban areas of England but in India it is more common in children belonging to rural population with a low socioeconomic status [5].

2.1.5 Coagulopathy

Some researches demonstrated an association of Perthes and coagulopathy involving protein C and S and hypofibrinolysis [17-19]. Following trauma these deficiencies may cause venous thrombus formation leading to femoral head infarction [1,9].

The current hypothesis [5] is that the child had genetic or acquired hypoplasia resulting in delayed bone age and the thick preossific cartilage of the femoral head which provides inadequate protection to the transferring vessels supplying the ossific epiphysis. The compression of the cartilage may reduce blood flow causing ischemia or infarction.

3. REVIEW OF MORPHOLOGY OF PERTHES DISEASE

From the large biopsies, it had been concluded [20] that in early stages "there was a more or less extensive avascular necrosis in the capital nucleus without any tissue reaction. In intermediate and later stages there was extensive repair with profuse formation of fibrous tissue and revascularization with cartilaginous bone formation. These outcomes were later confirmed by another study [21] which observed

that findings ranged from an ischaemic arrest of ossification in the capital articular cartilage without infarction to multiple complete infarctions of epiphyseal bone. The ensuing repairing process contributes to the pathology of Perthes.

It could not be predicted that which heads of femur would do well and which would not with conservative treatment. The literature suggested problem in the healing process (resorption and lack of anabolism) but the understanding of biology is missing [22]. To understand it, researchers [23] turned to animal model. The piglets have been the most studied model for Perthes because of its similar epiphyseal circulation. Therefore, it mimics the progression through fragmentation and reossification that occurs in humans. It was observed that there is a wide gap between resorption and bone anabolism. This led to the idea of using anti-resorptive agents and later use of bone anabolic agents [Bone morphogenic protein-2 (BMP-2)].

4. CLINICAL PRESENTATION

The onset of disease occurs usually in between 2-12 years with most cases occurring between 4-9 years. Males with smaller stature are more frequently involved. In majority of cases only single hip is involved. The commonest presentation is limp with mild, insidious pain felt at hip, thigh and knee. Furthermore, there are attacks of these symptoms with intermittent period of total normal [1]. The symptoms worsen with physical activities. Many times children present with a definite history of trauma to the hip region. The clinical signs include limp that is either antalgic or trendelenburg or combination of both. There is presence of gluteal and quadriceps wasting. There are restrictions of hip movements especially that of abduction and internal rotation. All the symptoms and signs increase with progression of disease which correlates with collapse of head of femur. If head remain spherical or ovoid, hip will remain as ball and socket joint with all range of movements whereas if head is flattened, the congruence of acetabulum will be lost and hip will become a 'rolling bearing' type joint with only flexion extension range of movements. However, if head is extruded, then the abduction will also be lost [1].

5. NATURAL COURSE OF THE DISEASE

The clinical course of the disease is very unpredictable. Initially, Walden-storm described the natural course of the LCDP into 4 stages: Initial stage, fragmentation, healing and residual stage [24]. It was further modified divided in 4 stages: Sclerotic, fragmentation, healing and healed stages [25]. It has been further observed that deformation of femoral head occurs during the late stage of fragmentation and early stage of revascularization [25]. However, during the synovitis stage the widening of joint space may be caused by synovitis or hypertrophy of articular cartilage. A smaller capital femoral epiphysis because of temporary cessation of endochondral ossification is caused by ischaemia. This is the earliest radiological sign. Fragmentation stage is characterized by appearance of radiolucencies within normal looking sclerotic head. The calcification in the lateral epiphysis is suggestive of lateral extrusion of soft, flattened and deformed head from the under cover of acetabulum. The metaphyseal changes (cysts) appear when unossified cartilage cells migrated into metaphysis. The healing phase is characterized by the appearance of subchondral bone which starts from periphery, center and anterior part are last to be reossify. Remodeling means the final shape of head femur at the skeletal maturity.

6. CLASSIFICATIONS

The extent of involvement or severity of disease can be classified using following classifications:

6.1 Catterall Classification

Based on the extent of epiphyseal involvement and percentage of collapse as seen in x-ray (both AP & Lateral views) [26,27]. In Group I, only anterior portion of epiphysis is involved. Group II, involves more of the anterior epiphysis with presence of central sequestrum with preservation of epiphyseal height. Group III, shows most of the epiphysis is sequestrated with unaffected portion being located medial or lateral to the central sequestrum. Group IV, shows sequestration of whole of the epiphysis.

6.2 Herring Classification

Classified the fragmentation stage into 3 groups. According to this classification head is divided into 3 pillars; medial, lateral and central. An intact lateral pillar acts as a weight bearing support to protect the central avascular segment. Group A, shows minimal density changes in lateral pillar with no loss of height loss, Group B shows loss of height of lateral pillar but less than half and

collapsed central segment is below the lateral pillar and Group C includes lateral column height loss is more than 50% with no separation of central and lateral segment [28].

6.3 Salter Thompson Classification

Based on subchondral fractures of femoral head due to stress on this area. When this subchondral fracture or 'Caffey's cresent sign' involve less than 50% of femoral head, it is grouped under 'A' and more than this is grouped in 'B' [29].

6.4 Modified Elizabeth Town Classification

The radiological classification of natural course of perthes disease, divided into four stages: (a) Sclerotic, which is further divided into no loss of height/loss of height (duration-220 days); (b) Fragmentation, which may be early/late (duration- 240 days); (c) Healing, which may be peripheral/>1/3 epiphysis (duration- 255 days) and (d) Healed.

Catterall classification was widely used in the past, but because of its application difficulty and high interobserver variability; its applicability and acceptance have gone down in recent literature [26,27]. However, due to the simplicity and prognostic value, Herring classification is being increasingly used by many authors [28].

7. DIAGNOSTIC EVALUATION

7.1 Plain X-rays

X-Rays AP & Lateral (frog) views of both hips are the first and most important investigations as it can tell the extent, staging, risk factors and progression and hence treatment can be decided.

7.2 Magnetic Resonance Imaging (MRI)

It is an accurate modality for the early diagnosis of Perthes. It can better evaluate the congruity of head, its containment, joint effusion and synovial hypertrophy. But its cost and infrequent availability are the limiting factors.

7.3 Bone Scan

Technetium scanning is an effective means of diagnosis of Perthes in its early stage. But early bone scan may at times suggest a more severe stage than really exists. Pinhole collimation in bone scans record the viability of lateral epiphysis and can predict the deformity [30,31].

7.4 Arthrography

The arthrogram is an important investigation for which intervention is being considered. An arthrogram may demonstrate whether the head is containable or non-containable. In non containable hips it may demonstrate the best position in which head is contained before the osteotomy. Catterall emphasizes the importance of arthrogram being dynamic [5].

8. PROGNOSTIC FACTORS: CATTERALL 'HEAD AT RISK' SIGNS

Catterall showed that 57% of untreated Perthes patients show good long term outcome. To determine which patients are likely to do better if left alone and which patients may be helped by surgical intervention, Catterall proposed following head at risk signs [27] to predict the prognosis- Clinical: progressive loss of movements, abduction contracture, flexion with abduction, overweight child and radiological: Gage sign, lateral calcification, lateral subluxation, metaphyseal cyst, and horizontal physis.

9. TREATMENT

Perthes is a self-healing disease characterized by temporary interruption of blood supply of head femur resulting into necrosis of the epiphysis. Complete revascularization and complete replacement of necrotic bone do occur in due course. The only justification of treatment is prevention of femoral head deformity and secondary degenerative osteoarthritis. If mechanical environment remain favorable, hip may recover a near normal shape and movements [5]. This could be made by reducing the forces acting through the hip [Fig. 1(a), (b), 1(c) & (d)].

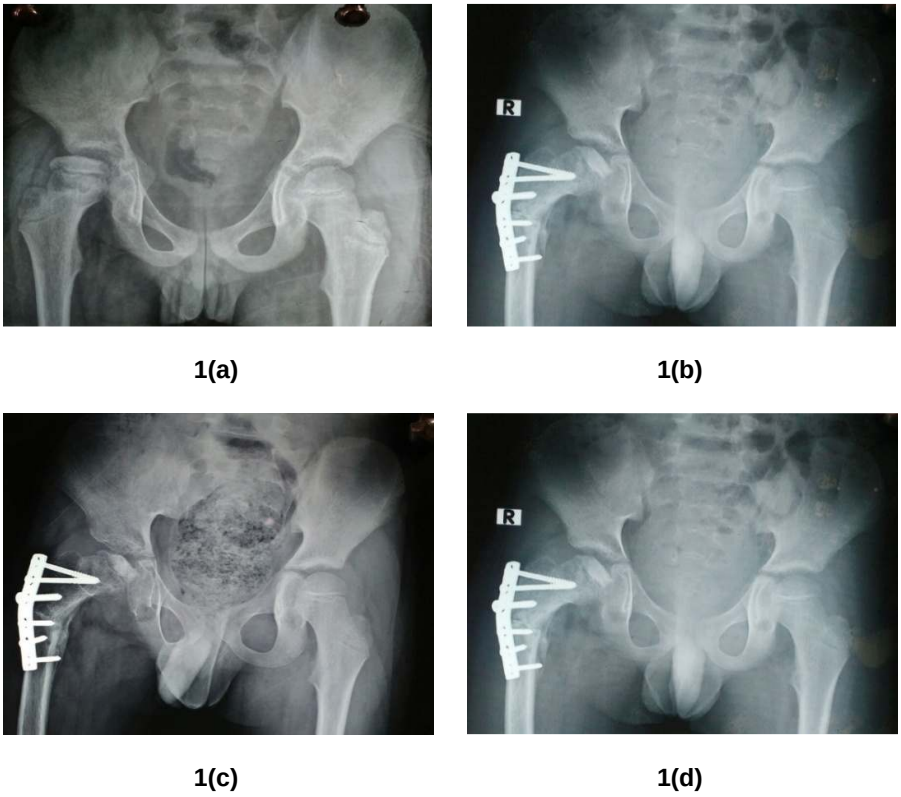
9.1 Pathogenesis and Timing of Femoral Head Deformation

The necrotic bone in femoral head may trigger the soft tissue changes, such as synovitis [32-35], articular cartilage hypertrophy [36] and hypertrophy of ligamentum teres [37]. These changes and muscular spasm may extrude the head out laterally of the acetabulum. This predisposes the exposed head to unusual

stresses during weight bearing. This result into trabecular collapse followed by irreversible femoral head deformation [38,39]. The lateral extrusion appears to be a prime factor that predisposes to the head deformation. If more than 20% of the width of epiphysis is extruded the head deformation is inevitable [40,41]. There is evidence that the femoral head deformation occurs during the last stage of fragmentation or in early stage of reconstitution [24]. It is emphasized that any treatment started at early stage may prevent the head deformation and if given at last stage of fragmentation (stage IIb) and thereafter is not preventive but either remedial or salvage in nature.

9.2 Treatment during Early Stage of Disease

Early stage of the disease is described from onset of disease to early part of fragmentation. During this stage attempts should be done to improve the containment of head by preventing or reversing the extrusion [32]. Containment means any intervention that places the antero-lateral part of femoral epiphysis well into the acetabulum so that it can be protected from the head deforming forces. Several studies suggest that the children above 6 years at onset of disease and in whom more than half of head epiphysis is involved are likely to benefit by containment [41-49]. Containment can be achieved by two methods; either by keeping the head in abduction and internal rotation or in flexion-abduction. This can be achieved either by casting, bracing or by surgery. Surgery can be done on femur by increasing the varus or can be achieved by surgery on ileum by an osteotomy that re-orients the acetabulum or by creating a bony shelf over the extruded part of the epiphysis. Contrary to earlier views that surgical containment has no effect on healing process [50,51]. It has been established that duration of the disease is significantly shortened by bypassing the stage of fragmentation when varus osteotomy is performed [45].



1(a) **1(b)**

1(c) **1(d)**

Fig. 1(a). Pre-operative image of a nine years old male suffering from Perthes Disease involving right hip; 1(b) Post-operative image at 2 months follow up; 1(c) Post-operative image at 5 months follow up; 1(d) Post-operative image at 15 months follow up

9.3 Treatment Planning

The variables to take into consideration to decide the treatment include age of the child at the onset of symptoms, the presence of extrusion of femoral head, the range of movements of hip and stage of disease [52]. The outline of decision making for treatment of Perthes' disease early in the course of disease has been shown in Table 1 [32]. The two widely used parameters; status of lateral pillar (Herring's grading) and extent of epiphysis involved (Catterall classification) is not included in the decision-making as treatment must be initiated well before the identification of these two parameters [53].

9.4 Non-operative Treatment

The majority of Perthes patients can be treated non-operatively. The force acting on the hip can be reduced by avoiding weight bearing or sports activity and use of crutches with toe touching walking. Swimming is recommended. The role of traction has been discussed by few workers [1-3]. They had advocated traction in flexion in this position the volume of hip is maximum, thus avoiding the complications raised by increased intra-articular pressure. The abduction of the limb can be maintained by keeping the limb in cast (broomstick cast, Petrie cast) or abduction braces (broomstick brace, Synder sling, Atlanta Scottish Rite Brace). These abduction measures have been used with varying reports of success [43-61]. The early reports were very encouraging by these workers, however, more recent studies did not show such favorable results [62-64]. Long term immobilization has negative consequences, including muscle atrophy, contractures, weight gain and social exclusion. It has been noted that a brace on radiograph is needed to ensure the right amount of abduction. Another conservative protocol consists of non weight bearing exercises at home with intermittent traction and Petrie cast has also not shown good results [32]. The results of no-treatment group were similar to those in the brace and range of movement group across all ages and degree of disease severity [64].

9.5 Operative Treatment

9.5.1 Proximal femoral varus osteotomy

By reducing neck shaft angle head of femur can be made better contained or centralized with in acetabulum. But it had several disadvantage such as scar mark, resurgery for implant removal and limb shortening. It has been observed that the outcome of varus osteotomy is no better than a non treated case after the age of 9 years [65]. Kim et al. [66] suggest 10-15°varus angulation is sufficient but Joseph et al. [45,52] suggest 20° varus angulation.

9.5.2 Innominate (Salter) osteotomy

It is a redirectional osteotomy of acetabulum which provides better coverage to the extruded part of head. The advantages over femoral varus osteotomy are in form of more acceptable scar and having no second surgery [67].

9.5.3 Triple pelvic osteotomy

It provides excellent coverage in elder children but there is a risk of overcoverage and pincer impingement. The acetabular fragment must not be rotated so far as to increase the CE angle beyond 44° when this osteotomy is performed [68].

9.5.4 Acetabular augmentation procedure

When the head is out of the stage of containment and is defined as when it extends beyond the confines of acetabulum. In such cases the coverage is extended by shelf procedure. It discourages the development of abduction hinge and may provide better cover later after a valgus osteotomy [5]. There is no study to determine the size of shelf to provide the adequate containment.

Table 1. Outline of decision-making for treatment of Perthes' disease early in the course of disease (Modified Elizabeth town classification) [32]

Variable	Contain	Don't contain
Age	>7 or <7 with extrusion	<7 (no extrusion)
Stage of evolution of the disease	Stage Ia, Ib, IIa	Stage IIb, IIIa, IIIb,IV
Extrusion	Present	Absent (<7 years)
Range of hip motion	Normal	Restricted

9.6 Treatment during Late Stage of Disease

Late stage is defined as late fragmentation and early stage of reconstitution. The modalities to treat these cases are aimed to minimize the effects early deformation which has already occurred.

9.6.1 Femoral valgus osteotomy

This osteotomy is aimed to overcome the abduction hinge. This brings more congruent part of head into acetabulum. But this osteotomy may increase the uncovering of femoral head [69]. Patient satisfaction following this procedure is very high as it provides an extra range of abduction with improved gait with an extra length of lower limb. It has been suggested that the results of this osteotomy are not so good if it is performed early with a plastic and deformable head femur [5].

9.6.2 Hip artrodiastasis

In attempt to unload the articular cartilage of head femur, artrodiastasis of hip by external fixator with or without soft tissue release has been used [4,70-72]. But all these studies are with medium followup and status of these hips at skeletal maturity is still to evaluate.

9.6.3 Multiple epiphyseal drillings

Multiple drilling has been done in the ischemic epiphysis with the hope that new vessels may grow into necrotic area through these channels. But long term follow up these hips is still awaited [73].

9.7 Treatment of the Sequela of the Disease

9.7.1 Cheilectomy/recreation of offset

In this procedure the extruded fragment is removed surgically [74]. However stiffness of the hip joint has been a frequent sequela and removal of the perichondral ring, together with the fragment, may resulted in slipped upper femoral epiphysis of the remaining epiphysis [5]. Recently, the operation has been repopularised by Benn group, who have performed it in association with trochantric distalisation with surgical dislocation of hip [75].

9.7.2 Total hip replacement

The secondary osteoarthritis hip can be managed by total hip replacement (THR). A number of complications are noted in some series, but survival rate of prosthesis is good [76-78].

In a prospective multicentric study [41] of the effect of treatment on outcome of Perthes, it was concluded that the lateral pillar classification and age at the time of onset of the disease strongly correlate with outcome in patients. Patients who are over the age of 8 years at the time of onset and have a hip in the lateral pillar B or B/C border group have a better outcome with surgical treatment than they do with nonoperative treatment. Group B hips in children less than 8 years of age at the time of onset have very favourable outcomes unrelated to treatment, whereas group C hips in children in all ages frequently have poor outcome, which also appear to be unrelated to treatment.

In a prospective clinical trial comparing the outcome of surgery and symptomatic surgery for patients presenting at age 5 years or younger [79], it was concluded that the Salter innominate osteotomy improves the outcome in the treatment of Cattrell 4/Herring C hips with lateral extrusion.

In a review of 172 cases [80] of Perthes with onset before 6 years of age, it was observed that prognosis for these patients are favourable with 80% having good results. Only children between the ages of 04 years and 5 years and 11 months with a B/C or C Herring hip have a less favourable prognosis. Treatment was not found to influence the outcome.

To evaluate the Head Reduction Osteotomy in the management in later stage of Perthes [81], a study concluded that this procedure can improve head sphericity. As well as can reduce pain. Avascular Necrosis (AVN) was not observed in any of these cases. In the same group .of cases, the role of relative neck lengthening was evaluated in 41 hips [82]. It was concluded that relative neck lengthening in hips with combined intra- and extraarticular impingement results in reduction in pain, improved hip function with improved radiological parameters. But long term results are still awaited.

10. RECENT TRENDS IN THE MANAGEMENT OF PERTHES

The perfusion MRI may hold promise in treatment planning and currently studies evaluating the efficiency of these imaging techniques are underway [83,84]. Intra-articular pressure measurements have revealed that immobilization in orthosis can elevate intra-articular pressure [85]. Few clinical trials have shown good results from use of vasoactive prostacycline analogues in early phase of disease, but results are still pending [86]. Few workers are studying the role of hip arthroscopy in selective cases of Perthes. Sometimes few patients complain of pain with possibility of loose body, in these cases arthroscopy can be very useful [87]. Role of bisphosphonate, BMP-2 and autologous stem cell in management of Perthes is still under investigation.

11. LONG TERM OUTCOME EVALUATION

İn the current literature most studies show results after conservative treatment. The long-term natural history of Perthes disease is not known. A deformed head femur will predispose the hip for secondary osteoarthritis. The Stulberg and Mose classification shows the shape of head in relation with acetabulum at skeletal maturity. Stulberg class I and II hip develops secondary osteoarthritis in long term; whereas class III and IV develops in late adult life. Stulberg V hip showing aspherical incongruency develops osteoarthritis early in life, before 50 years [88]. Children presenting at 6 years of age with head at risk signs are likely to ends up with Stulberg I and II whether they receive the treatment or not. Children with age more than 9 years at onset with whole head involvement will result into Stulberg III and IV irrespective of mode of treatment. A surgical intervention in children between 6-9 years may be beneficial and this intervention may result into Stulberg I and II. Stulberg I and II are capable to support their life with normal physical activity for at least 30 years of adult life. A study with long term follow up of Perthes, found that nearly 40% of hip eventually require THR, mostly between 40 and 60 years [89].

12. CONCLUSION

Perthes disease is a complex multifactorial paediatric disease without any known evidence based etiology. Though numerous classifications have been proposed for this disease, but none of them is based on its etiology and pathogenesis. A defenative stage wise treatment protocol to predict longterm outcomes of conservative and surgical modalities is still under review.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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